Complete Listing of Claims Pursuant to 37 C.F.R. §1.121

Pursuant to 37 C.F.R. §1.121 the following is a complete listing of the claims of the present application. In this set of claims, please amend claims 14, 29, 34, 36, and 39 as follows. With the amendments to the aforementioned claims, the following listing of claims will replace all prior versions, and listings, of claims in the application:

1. [cancelled] A formulation of a pharmaceutical composition comprising a human recombinant α-L-iduronidase or biologically active fragments or mutein thereof with a purity of greater than 99%, or in combination with a pharmaceutically suitable carrier.

2. [cancelled] The formulation of claim 1, wherein said recombinant α-L-iduronidase or biologically active fragments or mutein thereof with a specific activity of greater than about 240,000 units per milligram protein.

3. [cancelled] The pharmaceutical composition of claim 1 further comprising a sodium chloride solution, a buffer and polysorbate 80.

4. [cancelled] The pharmaceutical composition of claim 1 wherein said human recombinant α-L-iduronidase or mutein thereof is present at a concentration range of about 80 to 150 units per mL.

5. [cancelled] The pharmaceutical composition of claim 1 wherein said human recombinant α-L-iduronidase or mutein thereof is present at a concentration of about 100 units per mL.

6. [cancelled] The pharmaceutical composition of claim 3 wherein said sodium chloride solution is at a concentration of about 150 mM.

7. [cancelled] The pharmaceutical composition of claim 3 wherein said buffer is a sodium phosphate monobasic buffer at a concentration of about 92 mM.

8. [cancelled] The pharmaceutical composition of claim 3 wherein said buffer is a sodium phosphate dibasic buffer at a concentration of about 8 mM.

9. [cancelled] The pharmaceutical composition of claim 3 after dilution into the dosage form wherein said human albumin is present at a concentration of at least about 1 mg/mL.

10. [cancelled] The pharmaceutical composition of claim 9 wherein human albumin is used to prevent or reduce acute allergic or complement mediated reactions in said human subject.

11. [cancelled] The pharmaceutical composition of claim 3 wherein the pH of said solution is maintained at about 5.8.

12. [cancelled] The pharmaceutical composition of claim 3 wherein said polysorbate 80 is maintained at 10 μM/mL.

13. [cancelled] The pharmaceutical composition of claim 12 wherein said polysorbate is required to stabilize the protein in the final product.

14. [currently amended] A method of treating a human diseases caused all or in part by a deficiency in α-L-iduronidase, comprising the steps of:

(a) administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a human recombinant α-L-iduronidase of SEQ ID NO:2, or a biologically active fragment of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2 ~~or a mutant of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2~~, wherein said human recombinant α-L-iduronidase of SEQ ID NO:2, or the biologically active fragment ~~or mutant~~ thereof ~~in said pharmaceutically acceptable carrier~~ has a purity of greater than 99%, to a human subject in need thereof;

(b) optimizing said treatment by assessment of primary efficacy endpoints;

(c) optimizing said treatment by assessment of secondary efficacy endpoints;

(d) optimizing said treatment by assessment of tertiary efficacy endpoints; and

(e) optimizing treatment by assessment of safety endpoints.

15. [previously presented] The method of claim 14, wherein said primary efficacy endpoints are selected from the group consisting of percent predicted forced vital capacity and six-minute walk distance.

16. [previously presented] The method of claim 14, wherein said secondary efficacy endpoints are selected from the group consisting of apnea/hypopnea index, liver organ volume, disability score index, and joint range of motion.

17. [previously presented] The method of claim 14, wherein said tertiary efficacy endpoints are selected from the group consisting of urinary glycosaminoglycan levels, total respiratory event index, pain, joint range of motion, quality of life, growth in prepubertal patients, visual acuity, echocardiogram, and forced expiratory volume.

18. [currently amended] The method of claim 14, 58, 59 or 60 wherein the disease is mucopolysaccharidosis.

19. [currently amended] The method of claim 14, 58, 59 or 60 wherein the disease is mucopolysaccharidosis I.

20. [currently amended] The method of claim 14, 58, 59 or 60 wherein the disease is selected from the group consisting of: Hurler's disease, Scheie syndrome and Hurler-Scheie syndrome.

21. [previously presented] The method of claim 14 wherein said human subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

22. [currently amended] The method of claim 14, 58, 59 or 60 wherein a dose of at least about 100 units ~~per kilogram~~ said human recombinant α-L-iduronidase or biologically active fragment thereof per kilogram body weight is administered weekly to a patient suffering from said deficiency.

23. [previously presented] The method of claim 22, wherein said dose is administered over a four-hour infusion.

24. [currently amended] The method of claim 14, 58, 59 or 60 wherein said administering is a slow infusion of at least 3000 units ~~0.5 mg/kg~~ of said α-L iduronidase or fragment formulation for about an hour, followed by a rapid two-hour infusion ~~rate~~ of at least 122,000 units to achieve a dose of at least 125,000 units/kg or 100SIU/kg or 0.5mg/kg.

25. [currently amended] The method of claim 24 wherein said infusion is used to minimize complement ~~mediation~~ mediated clinical allergic reactions.

26. [currently amended] The method of claim 14 wherein said treatment with human recombinant α-L-iduronidase or biologically active fragment thereof reduces lysosomal storage of glycosaminoglycans (GAGs) in the tissue of said human subject caused all or in part by said deficiency in α-L-iduronidase.

27. [previously presented] The method of claim 14 wherein said treatment causes improvement in said endpoints of said human subjects.

28. [currently amended] The method of claim 14 wherein said treatment results in increase in percent forced vital capacity, increase in distance of six-minute walk, reduction of liver volume ~~and~~ or urinary glycosaminoglycan excretion, reduction in spleen size ~~and~~ or apnea/hypopnea events, increase in height ~~and~~ or growth velocity in prepubertal patients, improvement in shoulder flexion ~~and~~ or elbow ~~and~~ or knee extension, reduction in symptoms related to cardiac function, ~~and~~ or increase in endurance ~~and~~ or reduction of limitations of daily activities.

29. [currently amended] A method of treating human diseases caused all or in part by a deficiency in α-L-iduronidase, comprising the steps of:

(a) administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a purified human recombinant α-L-iduronidase of SEQ ID NO:2, or biologically active fragment of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2 ~~or a mutant of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2~~, wherein said human recombinant α-L-iduronidase of

SEQ ID NO:2, biologically active fragment ~~or mutant~~ thereof ~~in said pharmaceutically composition~~ has a purity of greater than about 99%, to a human subject in need thereof; and

(b) optimizing said treatment by evaluating biochemical and clinical symptoms of said subject through routine assessment of history, physical examination, echocardiography, electrocardiography, magnetic resonance imaging, polysomnography, skeletal survey, range of motion measurements, corneal photographs, ~~and~~ or skin biopsy.

30. [previously presented] The method of claim 29 wherein the disease is mucopolysaccharidosis.

31. [previously presented] The method of claim 29 wherein the disease is mucopolysaccharidosis I.

32. [previously presented] The method of claim 29 wherein the disease is selected from the group consisting of: Hurler's disease, Scheie syndrome and Hurler-Scheie syndrome.

33. [previously presented] The method of claim 29 wherein said subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

34. [currently amended] The method of claim 29 wherein a dose of at least about 125,000 units/kg body weight or 100 SIU/kg body weight or 0.5 mg/kg body weight of said human recombinant α-L-iduronidase or biologically active fragment is administered weekly to said human subject wherein said human subject is suffering from a deficiency thereof.

35. [currently amended] The method of claim 29 wherein said administering is a slow infusion of at least 3000 units ~~0.5 mg/kg~~ of said α-L iduronidase or fragment formulation for about an hour, followed by a rapid two-hour infusion ~~rate~~ of at least 122,000 units to achieve a dose of at least 125,000 units/kg or 100SIU/kg or 0.5mg/kg.

36. [currently amended] The method of claim 35 wherein said infusion is used to minimize complement ~~mediation~~ mediated clinical allergic reactions.

37. [currently amended] The method of claim 29 wherein said treatment with human recombinant α-L-iduronidase or biologically active fragment thereof reduces lysosomal storage of GAGs in the tissue of said human subject caused all or in part by said deficiency in α-L-iduronidase ~~of said human subjects~~.

38. [currently amended] The method of claim 29 wherein said treatment results in normalization of liver volume ~~and~~ or urinary glycosaminoglycan excretion, ~~and~~ or reduction in spleen size ~~and~~ or apnea/hypopnea events, ~~and~~ or increase in height ~~and~~ or growth velocity in prepubertal patients, ~~and~~ or increase in shoulder flexion ~~and~~ or elbow ~~and~~ or knee extension, ~~and~~ or reduction in tricuspid regurgitation or pulmonic regurgitation.

39. [currently amended] A method of treating diseases caused all or in part by a deficiency in α-L-iduronidase, comprising the steps of:

administering a pharmaceutical composition to a human subject in need thereof;

wherein said pharmaceutical composition comprises a purified human recombinant α-L-iduronidase of SEQ ID NO:2, or biologically active fragment of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2 ~~or, a mutant of SEQ ID NO:2 which possesses the same or similar biological activity to SEQ ID NO:2,~~ wherein said human recombinant α-L-iduronidase of SEQ ID NO:2, or biologically active fragment ~~or mutant~~ thereof in ~~said pharmaceutical composition~~ has a purity of greater than about 99%.

40. [previously presented] The method of claim 39 wherein the disease is mucopolysaccharidosis.

41. [previously presented] The method of claim 39 wherein the disease is mucopolysaccharidosis I.

42. [previously presented] The method of claim 39 wherein the disease is selected from the group consisting of: Hurler's disease, Scheie syndrome and Hurler-Scheie syndrome.

43. [previously presented] The method of claim 39 wherein said subject suffering from the disease demonstrates about 1% or less of a normal α-L-iduronidase activity.

44. [currently amended] The method of claim 39 wherein a dose of at least about 125,000 units/kg body weight or 100 SIU/kg body weight or 0.5 mg/kg body weight of said human recombinant α-L-iduronidase or biologically active fragment thereof is administered weekly ~~to a patient suffering from a deficiency thereof~~.

45. [currently amended] The method of claim 39 wherein said administering is the slow infusion of at least 0.5 mg/kg body weight of said ~~formulation~~ α-L-iduronidase or biologically active fragment thereof for about an hour, followed by a rapid two-hour infusion rate.

46. [currently amended] The method of claim 45 wherein said infusion is used to minimize complement ~~mediation~~ mediated clinical allergic reactions.

47. [currently amended] The method of claim 39 wherein said administering with human recombinant α-L-iduronidase or biologically active fragment thereof reduces lysosomal storage of GAGs in the tissues of said human subjects.

48. [previously presented] The method of claim 39 wherein said administering results in a decrease in the volume of the liver of said patient by at least 5%.

49. [previously presented] The method of claim 48 wherein said administering results in a decrease in the volume of the liver of said patient by at least 19%.

50. [previously presented] The method of claim 39 wherein said administering results in a decrease in the volume of the spleen of said patient by at least 13%.

51. [previously presented] The method of claim 39 wherein said administering results in a decrease in the urinary glycosaminoglycan excretion of said patient by at least 60%.

52. [previously presented] The method of claim 39 wherein said patient is a prepubertal patient and said administering results in an increase of the height growth velocity of said patient by at least 2.4 cm/year.

53. [previously presented] The method of claim 39 wherein said patient is a prepubertal patient and said administering results in an increase of the weight growth velocity of said patient by at least 2.4 kg/year.

54. [previously presented] The method of claim 39 wherein said administering results in an increase of the shoulder flexion of said patient.

55. [previously presented] The method of claim 39 wherein said administering results in an increase of the elbow and knee extension of said patient.

56. [previously presented] The method of claim 39 wherein said administering results in a reduction of apnea and hypopea events of said patient.

57. [previously presented] The method of claim 39 wherein said patient has tricuspid regurgitation or pulmonic regurgitation caused all or in part by a deficiency in α-L-iduronidase treatment and wherein said administering results in a reduction in said tricuspid regurgitation or pulmonic regurgitation.

58. [new] A method of treating a human disease caused all or in part by a deficiency in α-L-iduronidase, comprising administering to a subject presenting the symptoms of said disease a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a purified human recombinant α-L-iduronidase of SEQ ID NO:2, or a biologically active fragment of SEQ ID NO:2 which possesses the same or similar biological activity of a human recombinant α-L-iduronidase of SEQ ID NO:2, wherein said human recombinant α-L-iduronidase of SEQ ID NO:2, or biologically active fragment thereof in said pharmaceutical composition has a purity of about 99% or greater, in an amount effective to alleviate the symptoms of said deficiency in α-L-iduronidase.

59. [new] A method of treating a human disease caused all or in part by a deficiency in α-L-iduronidase, comprising administering to a human subject in need thereof a pharmaceutical composition comprising a purified human recombinant α-L-iduronidase of SEQ ID NO:2 and a pharmaceutically acceptable carrier, wherein said human recombinant α-L-iduronidase of SEQ ID NO:2 has a purity of about 99% or greater.

60. [new] A method of treating a human disease caused all or in part by a deficiency in α-L-iduronidase, comprising administering to a human subject in need thereof a pharmaceutical composition comprising a purified human recombinant α-L-iduronidase of SEQ ID NO:2 and a pharmaceutically acceptable carrier, wherein said human recombinant α-L-iduronidase of SEQ ID NO:2 has a purity of about 99.9% or greater.